

### **In the Claims**

1. (Withdrawn) DNA comprising one or more genes specific for 5S clavam biosynthesis in *S. clavuligerus* and which is not essential for 5R clavam biosynthesis.
2. (Withdrawn) DNA according to claim 1 as identified in Figure 1 (SEQ ID No: 1).
3. (Withdrawn) DNA according to claim 1 having the sequence or substantially the sequence shown in Figure 1 as orfup3, orfup2, orfup1, orfdwn1, orfdwn2 or orfdwn3 (SEQ ID Nos: 2-7).
4. (Withdrawn) DNA according to claim 1 having the sequence or substantially the sequence shown in Figure 1 as orfup1 (SEQ ID No: 4).
5. (Withdrawn) DNA which hybridises under conditions of high stringency with the DNA of claim 1.
6. (Withdrawn) A vector comprising the DNA of claim 1 in which one or more of the genes specific for 5S clavam biosynthesis has been disrupted or otherwise made defective.
7. (Withdrawn) A vector according to claim 6 containing one or more defective genes which is pCEC060, pCEC061, pCEC056 or pCEC057.
8. (Withdrawn) A vector according to claim 7 which is pCEC061.
9. (Withdrawn) A host containing the vector of claim 6.
10. (Withdrawn) A host according to claim 9 which is capable of producing raised levels of clavulanic acid.
11. (Withdrawn) A host according to claim 9 which is capable of producing low or no levels of 5S clavam.

12. (Withdrawn) A host according to claim 9 which is *S. clavuligerus*.
13. (Withdrawn) *S. clavuligerus* comprising DNA corresponding to an open reading frame flanking cas1 which DNA has been disrupted or otherwise made defective.
14. (Withdrawn) *S. clavuligerus* according to claim 13 wherein the open reading frame is selected from the group consisting of orfup3, orfup2, orfup1, orfdwn1, orfdwn2 and orfdwn3.
15. (Withdrawn) A process for improving 5R clavam production in a suitable microorganism comprising manipulation of DNA as defined in claim 1 and its inclusion in the microorganism.
16. (Withdrawn) A process according to claim 15 wherein said suitable microorganism is *S. clavuligerus*.
17. (Withdrawn) A process for improving 5R clavam production in *S. clavuligerus* comprising disrupting or otherwise making defective DNA regions flanking cas1.
18. (Withdrawn) A process according to claim 15 wherein said DNA corresponds to open reading frames selected from the group consisting of orfup3, orfup2, orfup1, orfdwn1, orfdwn2 and orfdwn3.
19. (Withdrawn) A process according to claim 15 wherein said DNA corresponds to open reading frame orfup1.
20. (Withdrawn) A process according to claim 15 wherein said 5R clavam is clavulanic acid.
21. (Withdrawn) A process for the identification of a microorganism suitable for high 5R clavam production comprising a preliminary screening for microorganisms with low or no 5S clavam production.

22. (Withdrawn) A process according to claim 21 wherein the microorganism is *S. clavuligerus*.
23. (Withdrawn) A process according to claim 22 wherein the 5R clavam is clavulanic acid.
24. (Withdrawn) A process according to claim 21 wherein one or more genes specific for the production of 5S clavams is defective.
25. (Withdrawn) A microorganism which is capable of 5R clavam production and low or no 5S clavam production obtainable by the process of claim 15.
26. (Withdrawn) A microorganism obtainable by the process of claim 25 which is capable of producing clavulanic acid but which does not produce clavam-2- carboxylate.
27. (Withdrawn) A microorganism obtainable by the process of claim 25 which is capable of producing clavulanic acid but which does not produce 2-hydroxymethylclavam.
28. (Withdrawn) A microorganism obtainable by the process of claim 25 which is capable of producing clavulanic acid but which does not produce clavam-2- carboxylate and 2-hydroxymethylclavam.
29. (Withdrawn) A microorganism obtained by the process of claim 15 which is strain 56-1A, 56-3A, 57-2B, 57-1C, 60-1A, 60-2A, 60-3A, 61-1A, 61-2A, 61-3A or 61-4A.

Claims 30-36 (Cancelled).

37. (Withdrawn) A process for the preparation of a composition comprising potassium clavulanate and amoxycillin which process comprises producing clavulanic acid from a microorganism according to claim 25 and thereafter converting it to the potassium salt and combining the potassium salt with amoxycillin.

Claims 38-44 (Cancelled).

45. (Presently Amended) A pharmaceutical composition which is free of one or more of the clavams selected from the group consisting of clavam-2-carboxylate, 2-hydroxymethylclavam, and 2-(3-~~alanyl~~alanyl)clavam comprising clavulanic acid, obtainable by the process comprising the steps of:

- (a) disrupting or otherwise making defective a DNA comprising one or more genes specific for 5S clavam biosynthesis in *S. clavuligerus* ~~a *Streptomyces*~~, selected from the group consisting of ~~orfup3 (SEQ ID NO: 2), orfup2 (SEQ ID NO: 3), orfup1 (SEQ ID NO: 4), orfdwn1 (SEQ ID NO: 5), orfdwn2 (SEQ ID NO: 6) and or-orfdwn3 (SEQ ID NO: 7)~~ ~~or a degenerate variant of orfup3 (SEQ ID NO: 2), orfup2 (SEQ ID NO: 3), orfup1 (SEQ ID NO: 4), orfdwn1 (SEQ ID NO: 5), orfdwn2 (SEQ ID NO: 6) or orfdwn3 (SEQ ID NO: 7);~~
- (b) fermenting said *S. clavuligerus* ~~a *Streptomyces*~~; and
- (c) purifying clavulanic acid therefrom.

46. (Cancelled)

47. (Presently Amended) The pharmaceutical composition according to claim ~~44~~ 45, wherein the clavulanic acid is in the form of a potassium salt.

48. (Presently Amended) The pharmaceutical composition according to claim ~~44~~ 45, further comprising a beta-lactam antibiotic.

49. (Presently Amended) The pharmaceutical composition according to claim ~~47~~ 48, wherein the beta-lactam antibiotic is amoxycillin.

50. (New) *Streptomyces* culture media comprising clavulanic acid and free of any 5S clavam as measured by HPLC analysis.

51. (New) The *Streptomyces* culture media according to claim 50 wherein the 5S clavam is selected from the group consisting of: clavam-2-carboxylate (C2C), 2-hydroxymethylclavam (2HMC), and 2-(3-alanyl)clavam (AC).